REMARKS

Applicants would like to express their appreciation to the Examiner for the courtesy extended to Joseph Kovarik and Angela Dallas in the telephone interview of June 5, 2001. During the interview, the rejection under 35 U.S.C. § 112, second paragraph was discussed. The Examiner suggested that the claims be amended to more clearly define the invention in terms of whether weight loss or weight gain is intended by any one method claim (e.g., by separating the method claims into two sets), and in terms of more particularly reciting what particular compounds and method steps are useful for weight loss or weight gain, respectively.

Applicants have attempted to address the Examiner's concerns by separating the claims into methods and compositions directed to weight loss (independent Claims 1, 59, 66, 68, 95 and 100) and into methods directed to weight gain (Claims 108-114). In addition, Applicants have amended the claims to more particularly recite the specific compound class that is useful for weight loss or weight gain, with regard to the particular method claimed. Finally, to expedite prosecution and to ease the review time required of the Examiner, Applicants have reduced the total number of claims from 107 to 66. Applicants expressly reserve the right to pursue the subject matter of any canceled claims in a continuation application.

Claim Amendments:

The amendments to the claims are largely clerical in nature and reflect a reduction in claim number and reorganization of the claimed subject matter as discussed above. However, support for certain of the claim amendments is found in the specification as follows.

With regard to Claim 1 and similarly amended claims, support for the amendment to recite a method for decreasing the body weight of an animal or reducing the rate of weight gain is found in original Claim 30, and in the specification, e.g., on page 24, lines 13-17; and , page 25, lines 3-5. Support for the amendment which recites "MSH or an MSH agonist" is found in original Claims 2-9 and in the specification, e.g., page 32, line 26, to page 33, line 3; page 33, lines 8-11; or page 33, line 17, to page 34, line 4. The phrase, "as compared to in the absence of administration of the compound" is supported in the specification, e.g., on page 64, lines 20-27; or page 68, lines 24-27.

With regard to Claim 108, support for the amendment to recite a method for increasing the body weight of an animal or reducing the rate of weight loss is found in original Claim 40 and in the

specification, e.g., on page 24, lines 13-17; or page 25, lines 5-9. Support for the amendment which recites "an MSH antagonist" is found in original Claims 41 and 45-50 and in the specification, e.g., page 33, lines 3-11; or page 34, lines 5-20. Dependent Claims 109, 110, 111, 112, and 113 are supported by original Claims 42, 47, 49, 50, and 107, respectively. Dependent Claim 114 is supported in the specification at page 30, lines 3-16.

Rejection of Claims 1-107 Under 35 U.S.C. § 112, Second Paragraph:

The Examiner has rejected Claims 1-107 under 35 U.S.C. § 112, second paragraph, contending that the claims indefinite. First, the Examiner contends that the meaning of the term "regulate" or the phrase "increase or decrease" body weight in the context of the claims is unclear, since, the Examiner asserts, animals can already regulated body weight to some degree. Therefore, the Examiner contends that it is unclear how one distinguishes background weight regulation from specific effects derived solely from the claimed method. Second, the Examiner contends that it is unclear how one method can both increase and decrease body weight. The Examiner suggested that the methods be claimed separately, as discussed above.

With regard to the first issue, Applicants initially note that the independent claims have been amended to add that the decrease or increase in the body weight of the animal is as compared to in the absence of administration of the compound. It is believed that this amendment clarifies that the effect is due to the administration of the MSH compound. In this regard, Applicants submit that the specification has demonstrated that the peripheral administration of an MSH compound according to the present invention is effective to decrease body weight and/or reduce weight gain, and that such effects are due to the administration of the MSH compound. By way of example, Examples 2-5 of the specification clearly shows that administration of an MSH agonist according to the present invention is effective to decrease the body weight of the mice as compared to in the absence of the compound. Referring to Example 2, since the genetically matched control mice were maintained on the same diet and activity level as the experimental mice, the effect was clearly substantially due to the peripheral administration of the MSH agonist and not to some other natural effect such as small degrees of weight gain or loss as a result of eating or exercise. Examples 3-5 provide additional evidence that reduction in body weight and/or a decrease in the rate of weight gain (e.g., see Example 5) are significantly attributable to the administration of the MSH analog.

With regard to the second issue, Applicants have adopted the Examiner's suggestion and have divided the method into separate claims directed to either decreasing body weight or increasing body weight. As discussed above, the claims have also been amended to recite the particular compounds useful in the respective methods.

In view of the foregoing discussion, Applicants respectfully request that the Examiner withdraw the rejection of Claims 1-107 under 35 U.S.C. § 112, second paragraph.

Applicants have tried to respond to all issues raised by the Examiner in the April 16, 2001 Office Action and submit that all pending claims are in condition for allowance. In the event that the Examiner has any questions or concerns regarding Applicants' position, the Examiner is invited to contact the below-named agent at (303) 863-9700.

Respectfully submitted,

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Date: July 16, 2001

Marked-Up Version Showing Amendments

Claims 2, 3, 11, 12, 14, 15, 17, 22, 30, 40-52, 57, 58, 60-65, 69, 71, 72, 76-79, 83, 84, 92, 96-97, 101 and 104-107 have been canceled.

Claims 1, 4, 6, 8-10, 13, 25-29, 31-39, 55, 56, 59, 66, 68, 70, 73-75, 80-82, 85-91, 95, 98, 100 and 102 have been amended as shown below.

Claims 5, 7, 16, 18-21, 23, 24, 53, 54, 67, 93, 94, 99 and 103 are pending and have not been amended.

Claims 108-114 have been added.

1. (Once Amended) A method to [regulate] decrease the body weight or reduce the rate of weight gain in an animal, comprising administering to said animal a therapeutic composition comprising [a proopiomelanocortin (POMC)] a melanocyte stimulating hormone (MSH) compound selected from the group consisting of MSH and an MSH agonist, wherein said [POMC] compound is administered to the periphery of said animal in an amount effective to measurably [regulate] decrease body weight or reduce the rate of weight gain in said animal as compared to in the absence of administration of said compound, whereby administration of said compound minimizes delivery of said compound to the central nervous system of said animal.

4. (Once Amended) The method of Claim 1, wherein said compound is selected from the group consisting of melanocyte stimulating hormone (MSH), a biologically active fragment of MSH, a homologue of MSH having MSH agonist activity, a peptide mimetic of MSH having MSH agonist activity, a non-peptide mimetic of MSH having MSH agonist activity, and a fusion protein comprising an MSH protein or a biologically active fragment thereof.

6. (Once Amended) The method of Claim 1, wherein said compound is a peptide mimetic of MSH having MSH agonist activity.

8. (Once Amended) The method of Claim 1, wherein said [POMC] compound is an α-MSH analog selected from the group consisting of:

a. [Ac-Cys^4, D-Phe^7, Cys^{10}] α-MSH, wherein said Cys residues are connected by a disulfide bond;

b. Ac-[Nle^4, X_{aa}^5, His^6, X_{aa}^7, Arg^7, Trp^9, X_{aa}^{10}]-NH_2, (SEQ ID NO:3)

wherein X_{aa}^5 is Glu or Asp, X_{aa}^7 is Phe or D-Phe and X_{aa}^{10} is a dibasic amino acid; Lys; ornithine; 2,4,-diaminobutyric acid; or 2,3 diaminopropionic acid (Dpr);

c. Ac-[Cys^4, Cys^{10}]α-$MSH_{1-13}NH_2$;

d. R_1-W-X-Y-Z-R_2,

wherein R_1 is selected from the group consisting of Ac-Gly-, Ac-Met-Glu-, Ac-Nle-Glu- and Ac-Tyr-Glu-;

W is selected from the group consisting of -His- and -D-His-;

X is selected from the group consisting of -Phe-, -D-Phe-, -Tyr, -D-Tyr-, (-pNO_2)D-Phe^7-;

Y is selected from the group consisting of -Arg- and -D-Arg-;

Z is selected from the group consisting of -Trp- and -D-Trp-; and,

R_2 is selected from the group consisting of -NH_2, -Gly-NH_2, and -Gly-Lys-NH_2;

e. Ac-Ser-Tyr-Ser-M-Glu-His-D-Phe-Arg-Trp-Gly-Lys-Pro-Val-NH_2 (SEQ ID NO:4),

wherein M is selected from the group consisting of Met, Nle, and Cys;

f. [Nle^4, D-Phe^7]-α-MSH;

g. [Nle^4, D-Phe^7]-α-MSH_{4-10};

h. [Nle^4, D-Phe^7]-α-MSH_{4-11};

i. [Nle^4, D-Phe^7,D-Trp^9]-α-MSH_{4-11};

j. [Nle^4, D-Phe^7]-α-MSH_{4-9}; and

k. Ac-[Nle^4, AA^5, D-Phe^7, AA^{10}]-R_1 or Ac-[Nle^4, AA^5, D-Phe^7, AA^{11}]-R_2;

wherein AA^5 may be either a L- or D- amino acid having an omega amino or carboxyl group in the side chain, e.g., α,γ-diaminopropionic acid, α,γ-diaminobutyric acid, Orn, Lys, α,β-aminoadipic acid, α-aminopimelic acid, or higher homologs, Glu or Asp;

wherein AA^{10} may be diaminopropionic acid, α,γ-diaminobutyric acid, Orn, Lys, α,β-aminoadipic acid, α-aminopimelic acid, or higher homologs, Glu or Asp;

wherein R_1 is the designation α-$MSH_{1-13}NH_2$, α-$MSH_{1-12}NH_2$, α-$MSH_{1-11}NH_2$, α-$MSH_{4-13}NH_2$, or α-$MSH_{4-10}NH_2$;

wherein AA^{11} may be L- or D- amino acid having an omega-amino or carboxyl group in the side chain, e.g., α,β-diaminopropionic acid; α,γ-diaminobutyric acid, Orn, Lys, α-aminoadipic acid, α-aminopimelic acid, or higher homologs, Glu or Asp;

wherein R_2 is the designation α-$MSH_{1-13}NH_2$, α-$MSH_{1-12}NH_2$, α-$MSH_{1-11}NH_2$, α-$MSH_{4-13}NH_2$, or α-$MSH_{4-10}NH_2$; and,

wherein Xxx may be from 1 to 5 a-amino acid residues each of which may be of L- or D- configuration, or a linear or branched chain spacer[;

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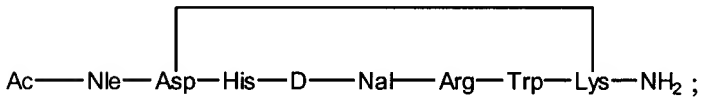

; and (SEQ ID NO:5)

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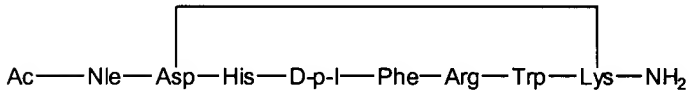

(SEQ ID NO:6); and,

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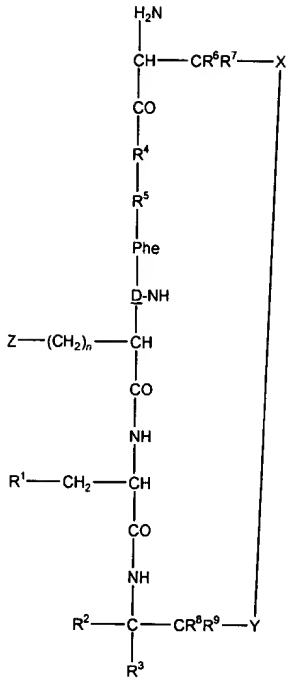


wherein R^1 is a substituted or unsubstituted aromatic radical;

R^2 is hydrogen or a methyl group;

R^3 is a carboxylate, carboxamide, hydroxymethyl, or aldehyde group;

R^4 is glutamic acid, alanine, -amino butyric acid, valine, leucine or isoleucine;

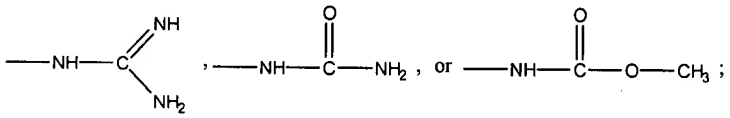
R^5 is histidine, glutamic acid, alanine, valine, leucine or isoleucine;

R^6 and R^7, which may be the same or different, are hydrogen, methyl or lower alkyl having one to five carbon atoms;

R^8 and R^9, which may be the same or different, are hydrogen, methyl or lower alkyl having one to five carbon atoms;

X and Y are sulfur, methylene, SO or SO_2;

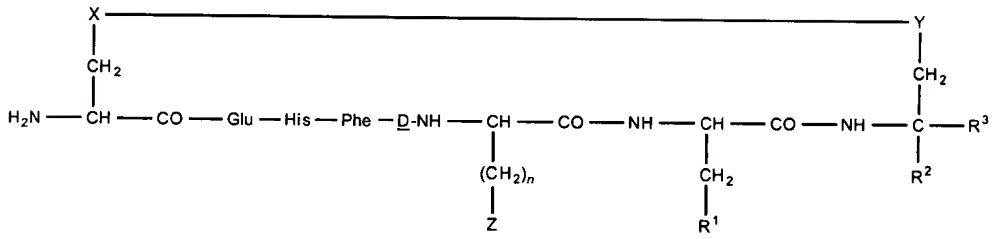
Z is $-NH_2$,



and,

n is an integer greater than or equal to 2;

o.



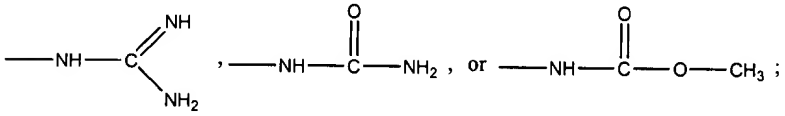
wherein R^1 is phenyl, indole, p-hydroxyphenyl, p-aminophenyl, imidazole, 1-naphthyl adamantyl or alkylphenyl, 2-naphthyl;

R^2 is hydrogen or a methyl group;

R^3 is a carboxylate, carboxamide, hydroxymethyl, or aldehyde group;

X and Y are sulfur, methylene, SO or SO_2;

Z is $-NH_2$,



and,

n is an integer greater than or equal to 2; and wherein the cyclized portion of the compound is conformationally restricted in a manner which is compatible with the reactivity of the compound with receptors of the central nervous system].

9. (Once Amended) The method of Claim 1, wherein said [POMC] compound is a peptide comprising an amino acid sequence represented by SEQ ID NO:1.

10. (Once Amended) The method of Claim 1, wherein said [POMC] MSH compound has the following identifying characteristics: (1) an ability to bind to [a POMC] a melanocortin receptor that is expressed in peripheral tissues; and, (2) a biological activity selected from the group consisting of stimulation of lipolysis and inhibition of the uptake of fatty acids by adipocytes.

13. (Once Amended) The method of Claim 1, wherein said compound binds to a melanocortin receptor expressed in the peripheral tissues [selected from the group consisting of MC2-R and melanocortin 5-receptor (MC5-R),] with a higher affinity than to melanocortin-4 receptors (MC4-R).

25. (Once Amended) The method of Claim 1, wherein said [POMC] compound is administered in a dose of from about 0.1 μg to about 10 mg per kg body weight of said animal.

26. (Once Amended) The method of Claim 1, wherein said [POMC] compound is administered in a dose of from about 1 μg to about 10 mg per kg body weight of said animal.

27. (Once Amended) The method of Claim 1, wherein said [POMC] compound is administered in a dose of from about 40 μg to about 1 mg per kg body weight of said animal.

28. (Once Amended) The method of Claim 1, wherein said [POMC] compound is from about 0.1% to about 90% of said therapeutic composition by weight.

29. (Once Amended) The method of Claim 1, wherein said [POMC] compound is from about 0.1% to about 1% of said therapeutic composition by weight.

31. (Once Amended) The method of Claim [30] 1, wherein said decrease in body weight in said animal can be measured within at least about one week of said step of administering said compound.

32. (Once Amended) The method of Claim [30] 1, wherein said animal has serum leptin levels between about 0 ng/ml and 50 ng/ml prior to said step of administration.

33. (Once Amended) The method of Claim [30] 1, wherein said animal has serum MSH levels between about 0 ng/ml and 10 ng/ml prior to said step of administration.

34. (Once Amended) The method of Claim [30] 1, wherein said animal has a ratio of serum MSH levels to serum leptin levels of greater than about 1:100 prior to said step of administration.

35. (Once Amended) The method of Claim [30] 1, wherein said animal is a human having a body mass index (BMI) of greater than 27 kilograms per square meter prior to administration of said compound.

36. (Once Amended) The method of Claim [30] 1, wherein said composition further comprises another body weight regulating agent.

37. (Once Amended) The method of Claim 36, wherein said another body weight regulating agent is leptin.

38. (Once Amended) The method of Claim [38] 37, wherein said composition comprises a ratio of said [POMC] MSH compound to leptin of about 1:100.

39. (Once Amended) The method of Claim [38] 37, wherein said composition comprises said leptin in a dose of from about 0.1 μg to about 100 mg per kg body weight of said animal.

55. (Once Amended) The method of Claim 1, wherein said composition further comprises an agent that inhibits binding of said [POMC] MSH compound to an MC4-R.

56. (Once Amended) The method of Claim 1, wherein said composition further comprises an agent which inhibits said [POMC] MSH compound from entering the central nervous system of said animal.

59. (Once Amended) A method of [regulating] decreasing the body weight or reducing the rate of weight gain in [of] an animal, comprising administering to an animal a [POMC] melanocyte stimulating hormone (MSH) compound selected from the group consisting of MSH and an MSH agonist in an amount effective to bind to [POMC] melanocortin receptors expressed by said animal in said animal's peripheral tissues, said effective amount:

(a) being insufficient to substantially change the appetite of said animal after said step of administering as compared to before said step of administering;

(b) being between about 0.1 μg and about 10 mg per kg of body weight of said animal;

(c) being sufficient to affect a biological activity selected from the group consisting of:

(i) lipolysis; and,

(ii) uptake of fatty acids by adipocytes in said animal; and,

(d) being effective to measurably [increase or] decrease the body weight or reduce the rate of weight gain of said animal after said compound has been administered to said animal.

66. (Once Amended) A method for regulating metabolic efficiency in an animal, comprising:

(a) measuring serum melanocyte stimulating hormone (MSH) levels in an animal;

(b) identifying animals having serum MSH levels of less than about 0.1 ng/ml; and,

(c) administering to the periphery of said animals identified in (b) a composition comprising a compound selected from the group consisting of a [POMC] melanocyte stimulating hormone (MSH) compound selected from the group consisting of MSH and an MSH agonist, and leptin, wherein said MSH compound is administered in an amount effective to increase serum MSH levels in said animal to a level effective to produce a result selected from the group consisting of stimulating lipolysis and inhibiting fatty acid uptake in said animal.

68. (Once Amended) A therapeutic composition that regulates the peripheral melanocortinergic and/or leptinergic pathways of energy homeostasis in an animal, comprising:

a. a [first body weight regulating agent that is a proopiomelanocortin (POMC)] melanocyte stimulating hormone (MSH) compound selected from the group consisting of MSH and an MSH agonist; and,

b. a [second] body weight regulating agent that is not a [proopiomelanocortin (POMC)] MSH compound.

70. (Once Amended) The therapeutic composition of Claim 68, wherein said [POMC] MSH compound is selected from the group consisting of melanocyte stimulating hormone (MSH), a biologically active fragment of MSH, a homologue of MSH having MSH agonist activity, a peptide mimetic of MSH having MSH agonist activity, a non-peptide mimetic of MSH having MSH agonist activity, and a fusion protein comprising an MSH protein or a biologically active fragment thereof.

73. (Once Amended) The therapeutic composition of Claim 68, wherein said [POMC] MSH compound is an analog of a peptide having an amino acid sequence represented herein by SEQ ID NO:2.

74. (Once Amended) The therapeutic composition of Claim 68, wherein said [POMC] MSH compound is an α-MSH analog selected from the group consisting of:

a. [Ac-Cys^4, D-Phe^7, Cys^{10}] α-MSH, wherein said Cys residues are connected by a disulphide bond;

b. Ac-[Nle^4, $X_{aa}{}^5$, His^6, $X_{aa}{}^7$, Arg^7, Trp^9, $X_{aa}{}^{10}$]-NH_2, (SEQ ID NO:3)

wherein $X_{aa}{}^5$ is Glu or Asp, $X_{aa}{}^7$ is Phe or D-Phe and $X_{aa}{}^{10}$ is a dibasic amino acid; Lys; ornithine; 2,4,-diaminobutyric acid; or 2,3 diaminopropionic acid (Dpr);

c. Ac-[Cys^4, Cys^{10}]α-$MSH_{1-13}NH_2$;

d. R_1-W-X-Y-Z-R_2,

wherein R_1 is selected from the group consisting of Ac-Gly-, Ac-Met-Glu-, Ac-Nle-Glu- and Ac-Tyr-Glu-;

W is selected from the group consisting of -His- and -D-His-;

X is selected from the group consisting of -Phe-, -D-Phe-, -Tyr, -D-Tyr-, (-pNO_2)D-Phe^7-;

Y is selected from the group consisting of -Arg- and -D-Arg-;

Z is selected from the group consisting of -Trp- and -D-Trp-; and,

R_2 is selected from the group consisting of -NH_2, -Gly-NH_2, and -Gly-Lys-NH_2;

e. Ac-Ser-Tyr-Ser-M-Glu-His-D-Phe-Arg-Trp-Gly-Lys-Pro-Val-NH_2 (SEQ ID NO:4),

wherein M is selected from the group consisting of Met, Nle, and Cys;

f. [Nle^4, D-Phe^7]-α-MSH;

g. [Nle^4, D-Phe^7]-α-MSH_{4-10};

h. [Nle^4, D-Phe^7]-α-MSH_{4-11};

i. [Nle^4, D-Phe^7,D-Trp^9]-α-MSH_{4-11};

j. [Nle^4, D-Phe^7]-α-MSH_{4-9}; and

k. Ac-[Nle^4, AA^5, D-Phe^7, AA^{10}]-R_1 or Ac-[Nle^4, AA^5, D-Phe^7, AA^{11}]-R_2;

wherein AA^5 may be either a L- or D- amino acid having an omega amino or carboxyl group in the side chain, e.g., α,γ-diaminopropionic acid, α,γ-diaminobutyric

acid, Orn, Lys, α,β-aminoadipic acid, α-aminopimelic acid, or higher homologs, Glu or Asp;

wherein AA^{10} may be diaminopropionic acid, α,γ-diaminobutyric acid, Orn, Lys, α,β-aminoadipic acid, α-aminopimelic acid, or higher homologs, Glu or Asp;

wherein R_1 is the designation α-$MSH_{1-13}NH_2$, α-$MSH_{1-12}NH_2$, α-$MSH_{1-11}NH_2$, α-$MSH_{4-13}NH_2$, or α-$MSH_{4-10}NH_2$;

wherein AA^{11} may be L- or D- amino acid having an omega-amino or carboxyl group in the side chain, e.g., α,β-diaminopropionic acid; α,γ-diaminobutyric acid, Orn, Lys, α-aminoadipic acid, α-aminopimelic acid, or higher homologs, Glu or Asp;

wherein R_2 is the designation α-$MSH_{1-13}NH_2$, α-$MSH_{1-12}NH_2$, α-$MSH_{1-11}NH_2$, α-$MSH_{4-13}NH_2$, or α-$MSH_{4-10}NH_2$; and,

wherein Xxx may be from 1 to 5 a-amino acid residues each of which may be of L- or D- configuration, or a linear or branched chain spacer[;

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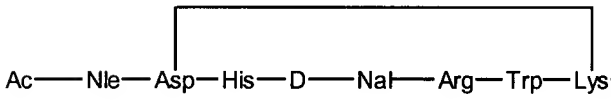

; and (SEQ ID NO:5)

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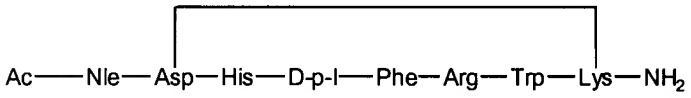

(SEQ ID NO:6); and,

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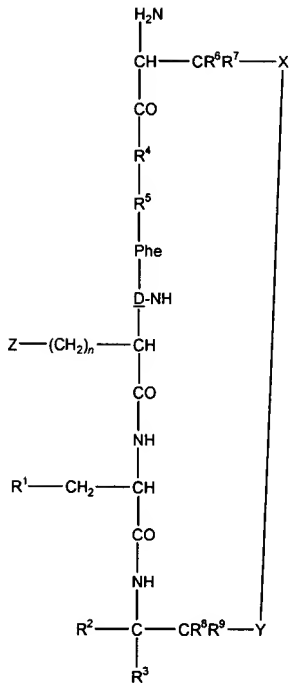


wherein R^1 is a substituted or unsubstituted aromatic radical;

R^2 is hydrogen or a methyl group;

R^3 is a carboxylate, carboxamide, hydroxymethyl, or aldehyde group;

R^4 is glutamic acid, alanine, -amino butyric acid, valine, leucine or isoleucine;

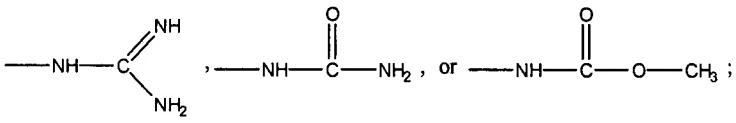
R^5 is histidine, glutamic acid, alanine, valine, leucine or isoleucine;

R^6 and R^7, which may be the same or different, are hydrogen, methyl or lower alkyl having one to five carbon atoms;

R^8 and R^9, which may be the same or different, are hydrogen, methyl or lower alkyl having one to five carbon atoms;

X and Y are sulfur, methylene, SO or SO_2;

Z is $-NH_2$,



and,

n is an integer greater than or equal to 2;

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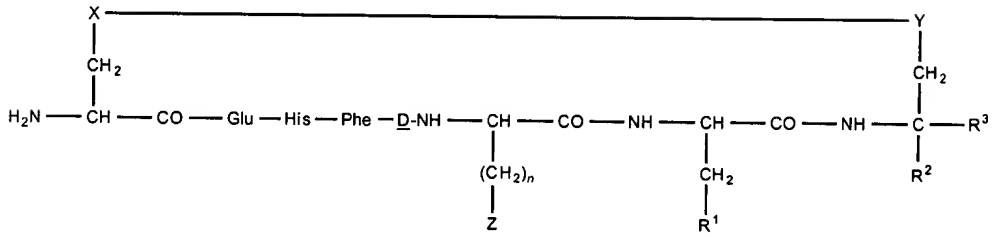


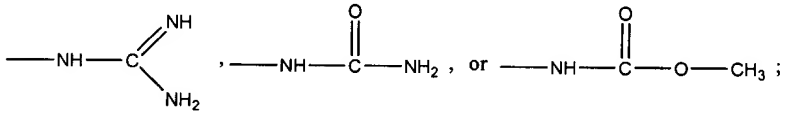
wherein R^1 is phenyl, indole, p-hydroxyphenyl, p-aminophenyl, imidazole, 1-naphthyl adamantyl or alkylphenyl, 2-naphthyl;

R^2 is hydrogen or a methyl group;

R^3 is a carboxylate, carboxamide, hydroxymethyl, or aldehyde group;

X and Y are sulfur, methylene, SO or SO_2;

Z is $-NH_2$,



and,

n is an integer greater than or equal to 2; and wherein the cyclized portion of the compound is conformationally restricted in a manner which is compatible with the reactivity of the compound with receptors of the central nervous system].

75. (Once Amended) The therapeutic composition of Claim 68, wherein said [POMC] MSH compound is a peptide comprising an amino acid sequence represented by SEQ ID NO:1.

80. (Once Amended) The therapeutic composition of Claim 68, wherein said composition comprises said [POMC] MSH compound in a dose of from about 0.1 μg to about 10 mg MSH compound per kg body weight of an animal to which said composition is to be administered.

81. (Once Amended) The therapeutic composition of Claim 68, wherein said composition comprises said [POMC] MSH compound [is administered] in a dose of from about 1 μg to about 10 mg MSH compound per kg body weight of an animal to which said composition is to be administered.

82. (Once Amended) The therapeutic composition of Claim 68, wherein said composition comprises said [POMC] MSH compound [is administered] in a dose of from about 40 μg to about 1 mg MSH compound per kg body weight of an animal to which said composition is to be administered.

85. (Once Amended) The therapeutic composition of Claim 68, wherein said [second] body weight regulating agent is leptin.

86. (Once Amended) The therapeutic composition of Claim 85, wherein said composition comprises a ratio of said [POMC] MSH compound to leptin of 1:100.

87. (Once Amended) The therapeutic composition of Claim 85, wherein said composition comprises a ratio of said [POMC] MSH compound to leptin of 1:25.

88. (Once Amended) The therapeutic composition of Claim 85, wherein said composition comprises a ratio of said [POMC] MSH compound to leptin of 1:10.

89. (Once Amended) The therapeutic composition of Claim 85, wherein said composition comprises said leptin in a dose of from about 0.1 μg to about 100 mg leptin per kg body weight of [said] an animal to which said composition is to be administered.

90. (Once Amended) The therapeutic composition of Claim 85, wherein said composition comprises said leptin in a dose of from about 0.1 μg to about 10 mg leptin per kg body weight of [said] an animal to which said composition is to be administered.

91. (Once Amended) The therapeutic composition of Claim 85, wherein said composition comprises said leptin in a dose of from about 1 μg to about 10 mg leptin per kg body weight of [said] an animal to which said composition is to be administered.

95. (Once Amended) A method for treating an affective and mood disorder in an animal, comprising administering to an animal at risk for or suffering from an affective mood disorder a therapeutic composition comprising a [proopiomelanocortin (POMC)] melanocyte stimulating hormone (MSH) compound selected from the group consisting of MSH and an MSH agonist, wherein said [POMC] MSH compound is administered to the periphery of said

animal in an amount effective to measurably ameliorate said disorder in said animal as compared to in the absence of administration of said compound, whereby administration of said compound minimizes delivery of said compound to the central nervous system of said animal.

98. (Once Amended) The method of Claim 1, wherein said animal is at risk for or [A method to treat an obesity-associated disorder in an animal, comprising administering to an animal] suffering from [or at risk for] an obesity-associated disorder [a therapeutic composition comprising a proopiomelanocortin (POMC) compound, wherein said POMC compound is administered to the periphery of said animal in an amount effective to measurably decrease body weight or to reduce the rate of weight gain in said animal, whereby administration of said compound minimizes delivery of said compound to the central nervous system of said animal].

100. (Once Amended) A method for treating a reproductive disorder in an animal, comprising administering to an animal at risk for or suffering from a reproductive disorder a therapeutic composition comprising a [proopiomelanocortin (POMC)] melanocyte stimulating hormone (MSH) compound selected from the group consisting of MSH and an MSH agonist, wherein said [POMC] MSH compound is administered to the periphery of said animal in an amount effective to prevent or ameliorate said disorder as compared to in the absence of administration of said compound, whereby administration of said compound minimizes delivery of said compound to the central nervous system of said animal.

102. (Once Amended) The method of Claim 1, wherein said animal is [A method to control undesired body weight which is a side effect resulting from administration of a pharmaceutical compound, comprising administering to an animal] at risk of or suffering from undesired body weight which is a side effect resulting from administration of a pharmaceutical compound[, a therapeutic composition comprising a proopiomelanocortin (POMC) compound wherein said POMC compound is administered to the periphery of said animal in an amount effective to measurably decrease body weight or weight gain in said animal, whereby administration of said compound minimizes delivery of said compound to the central nervous system of said animal].

108. (Added) A method to increase the body weight or reduce the rate of weight loss in an animal, comprising administering to said animal a therapeutic composition comprising a melanocyte stimulating hormone (MSH) antagonist compound, wherein said compound is administered to the periphery of said animal in an amount effective to measurably increase body weight or reduce the rate of weight loss in said animal as compared to in the absence of administration of said compound, whereby administration of said compound minimizes delivery of said compound to the central nervous system of said animal.

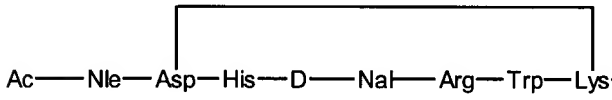
109. (Added) The method of Claim 108, wherein said compound has the following identifying characteristics: (1) an ability to bind to a melanocortin receptor that is expressed in peripheral tissues of said animal; and, (2) a biological activity selected from the group consisting of inhibition of lipolysis and stimulation of the uptake of fatty acids by adipocytes.

110. (Added) The method of Claim 108, wherein said MSH antagonist compound is selected from the group consisting of a fragment of MSH having MSH antagonist activity, a homologue of MSH having MSH antagonist activity, a peptide mimetic of MSH having MSH antagonist activity, a non-peptide mimetic of MSH having MSH antagonist activity, and a fusion protein comprising a peptide having MSH antagonist activity.

111. (Added) The method of Claim 108, wherein said antagonist compound is a peptide mimetic of MSH having MSH antagonist activity.

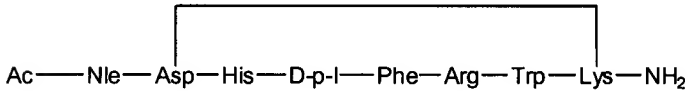
112. (Added) The method of Claim 108, wherein said antagonist compound is an MSH analog selected from the group consisting of:

a.



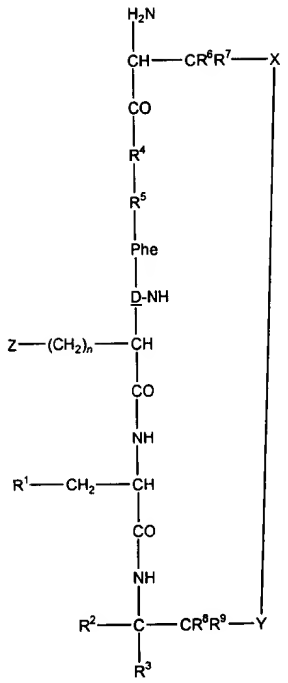
; and (SEQ ID NO:5)

b.



(SEQ ID NO:6); and,

c.



wherein R^1 is a substituted or unsubstituted aromatic radical;

R^2 is hydrogen or a methyl group;

R^3 is a carboxylate, carboxamide, hydroxymethyl, or aldehyde group;

R^4 is glutamic acid, alanine, -amino butyric acid, valine, leucine or isoleucine;

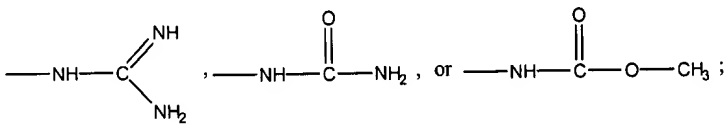
R^5 is histidine, glutamic acid, alanine, valine, leucine or isoleucine;

R^6 and R^7, which may be the same or different, are hydrogen, methyl or lower alkyl having one to five carbon atoms;

R^8 and R^9, which may be the same or different, are hydrogen, methyl or lower alkyl having one to five carbon atoms;

X and Y are sulfur, methylene, SO or SO_2;

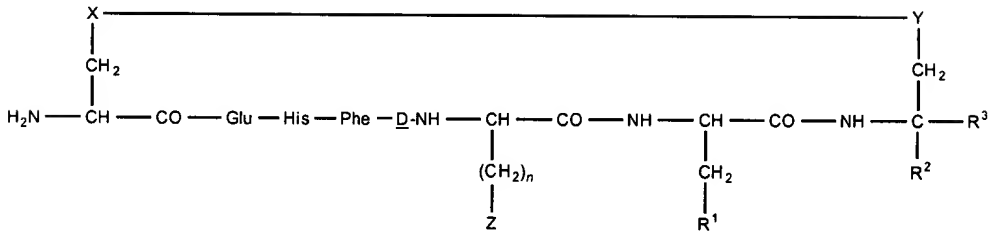
Z is $-NH_2$,



and,

n is an integer greater than or equal to 2; and,

d.



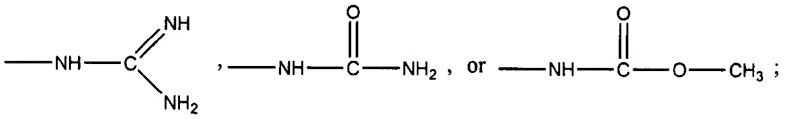
wherein R^1 is phenyl, indole, p-hydroxyphenyl, p-aminophenyl, imidazole, 1-naphthyl adamantyl or alkylphenyl, 2-naphthyl;

R^2 is hydrogen or a methyl group;

R^3 is a carboxylate, carboxamide, hydroxymethyl, or aldehyde group;

X and Y are sulfur, methylene, SO or SO_2;

Z is $-NH_2$,



and,

n is an integer greater than or equal to 2; and wherein the cyclized portion of the compound is conformationally restricted in a manner which is compatible with the reactivity of the compound with receptors of the central nervous system.

113. The method of Claim 108, wherein said animal suffers from an eating disorder selected from the group consisting of anorexia and bulemia.

114. The method of Claim 108, wherein said animal suffers from a wasting syndrome selected from the group consisting of: wasting disease, cachexia and sarcopenia.